AN ACCOUNT

OF THE

EPIDEMIC OUTBREAK OF ARSENICAL POISONING

OCCURRING IN

BEER DRINKERS IN THE NORTH OF ENGLAND AND THE MIDLAND COUNTIES IN 1900

BY

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For the last twelve months I noticed, both in the medical wards of the Manchester Workhouse Infirmary and in the out-patient department of the Manchester Royal Infirmary, a considerable number of cases presenting unusual skin eruptions of a more or less indefinite character, such as erythema, keratosis, and pigmentation,

the last being particularly common among the pauper patients. Some of the pigmented cases were diagnosed as Addison's disease by my assistants, but I could never satisfy myself that this diagnosis was correct. In June, 1900, about six patients presented themselves in one week who were suffering from the typical erythromelalgia or painful red neuralgia of Weir Mitchell, not only the feet but in some cases the hands also being affected; so marked were these cases that in June I gave a clinical lecture on the condition to the students of the Manchester Royal Infirmary. During the last seven months, I noticed a remarkable increase in the number of cases of herpes zoster, which appeared to be in epidemic form, and during this period I saw probably more cases than I had seen altogether in the past two years.

At the beginning of August quite an extraordinary number of cases of so-called "alcoholic paralysis" were admitted into the workhouse hospital, principally among women. So-called alcoholic peripheral neuritis is a fairly common disease in the Manchester district, very much more common as I understand than in London and the south, and perhaps I may be excused for saying that we are specially well acquainted with the affection, for it was principally owing to the work of our physicians Dr. Dreschfeld and the late Dr. J. Ross, that such excellent descriptions were given to the medical world. By it we understand a peripheral neuritis associated with paræsthesiæ and numbness in the hands and feet, paralysis of the arms and legs, cramps of the muscles, and especially great pain on pressure of the muscular masses of the limbs; in addition there is frequently a dilated left heart with cardiac muscle failure, and marked œdema of the trunk and legs and often albuminuria; very rarely indeed, almost never, is there any affection of the cranial nerves. In some cases there is an almost characteristic mental condition with loss of memory for time and place. It may be at once mentioned that the only forms of peripheral neuritis associated with great pain on muscular

pressure are, the alcoholic,[1] the arsenical, and that form found in beri-beri.

This great increase in the number of cases of alcoholic neuritis was noted by many observers, some of whom thought that it was due to increased drinking, owing to the war fever, or to a wrongful expenditure of the money given by the charitable towards the war funds. There was at the beginning of November no longer any doubt that a serious epidemic existed not only in Manchester and Salford, but also in neighbouring towns. Now, rightly or wrongly,—and this is a matter far too large and important to discuss in this paper,—I have for many years doubted whether ethylic alcohol *per se* does cause peripheral neuritis at all, and I have personally felt more confirmed in this opinion each succeeding year. I was therefore, in the present epidemic, not content with the alcoholic theory, but was at once on the look-out for some other possible cause of the neuritis. I could not at first find a satisfactory explanation, but at any rate I confirmed a previous opinion,[2] that in this district alcoholic neuritis only occurred among beer drinkers, not amongst pure spirit drinkers. Then we noticed at the workhouse, that the peculiar skin lesions already mentioned in passing were very often found in the patients who were suffering from neuritis; secondly a few cases of beautiful herpes zoster were found in the neuritic cases. Thereupon I remembered that arsenic was the only known drug which produced herpes, and so if there was any known drug acting as a poison in the beer it was almost certainly arsenic.

Improbable as this hypothesis at first seemed, yet it was a valid hypothesis, for it was not known to be untrue, it explained all the facts, and it was easily capable of proof or disproof. This hypothesis I imagined on November 15th, 1900. On November 17th I obtained some of the beer most commonly partaken of by the

[1] By "alcohol paralysis" or neuritis in this paper I mean *so-called* alcoholic paralysis or neuritis.

[2] See 'Medical Chronicle,' June, 1890, p. 189.

sufferers, and on November 18th, by Reinsch's test, I easily obtained a deposit on the copper foil, and driving this off in a combustion tube, I got well-marked crystals of arsenious oxide, and thus the hypothesis became a fact.

Source of the arsenic.—On speaking to Dr. H. A. G. Brooke about the skin lesions he told me that he was treating a young London hop merchant for similar eruptions, and by his kindness I saw the patient with him, and we found that he had undoubtedly got slight arsenical poisoning, although he took very little beer; but he frequently chewed hops, and we concluded that the sulphur with which the hops were treated would be found to be the source of the arsenic. This was soon found, however, not to be the cause of the present epidemic, especially as so little hops are used in making cheap beers. I have, however, been informed that the sulphur is often contaminated with arsenic, and in this way hops on the market often yield a reaction showing the presence of traces of arsenic, thus accounting for the symptoms in a gentleman constantly tasting them. I communicated my discovery of the arsenic to Professor Dixon Mann on November 19th, and on November 20th he examined a different sample of beer and also found arsenic. He informed Professor S. Delépine, who was, unknown to me, also investigating the epidemic at the request of Mr. C. H. Tattersall, the medical officer of health of Salford, and he, on November 22nd, traced the arsenic to certain sugars used in brewing. These were invert sugar, made by the action of sulphuric acid on cane sugar, and glucose, made by the action of sulphuric acid on various forms of starch. It was easy to see that the sulphuric acid was the common source of the arsenic, and on being examined large quantities were found, the original source being the Spanish pyrites from which the sulphuric acid is made, and which often contains a very large percentage of arsenic. As it happened, the brewing sugars from one firm only were found to be thus

contaminated, but as this firm supplies no less than 200 breweries in the North of England and Midland Counties, it will be seen how wide-spread the epidemic was likely to be.

Quantitative analyses.—By the kindness of Professor Delépine, I am able to give some interesting quantitative determinations, the arsenic being estimated as arsenious oxide. Various beers were found to contain from two to over four parts per million, that is from 0·14 to 0·3 grain per gallon. The invert sugar contained 0·25 part per 1000, the glucose 0·8 part per thousand, and the sulphuric acid no less than 1·4 per cent., or four ounces per gallon.

Other sources of arsenic.—From a legal and commercial point of view these results are of the highest importance, but from a scientific point of view it is equally important to know that traces of arsenic may get into beer from other sources. I have already mentioned that it is contained in sulphured hops; it is also found in many samples of malt, getting there either from sulphur or from anthracite coal; it has been found by Dr. John Brown, of Bacup, in the vulcanite tubing used for conveying the beer to the pumps. Again, calcium bisulphate and sulphuric acid are used in "fining" the beer, and also, I believe, for cleansing the barrels. Another point worth recording is that many artificial manures are contaminated with arsenic. A possible explanation of the manner in which arsenic may be retained in beer during the various processes, and may be of peculiar virulence, is that, according to the researches of Selmi, Hamberg, Sanger, Saccardo and others,[1] certain micro-organisms, especially *Aspergillum glaucum, Mucor mucedo,* and *Penicillium brevicaule,* seem to have a special tendency to seize hold of any arsenic in their vicinity, and to manufacture specially poisonous arsenical products. This has so far been worked out more particularly in connection

[1] Allbutt's 'System of Medicine,' vol. ii, p. 989.

with arsenical wall papers, but, as Dr. R. T. Williamson [1] points out, it is very desirable that further researches on these arsenio-bacteria should be made.

Extent of the epidemic.—Although the epidemic seems to have fallen most heavily on Manchester and Salford, and the vicinity, yet many more distant towns in the North of England and the Midlands have been affected,—wherever indeed the contaminated brewing sugars were used. Thus we hear of outbreaks in Liverpool, Chester (where the cases were associated with so much heart failure and so little pigmentation that they were diagnosed as beri-beri), Warrington, Heywood, Bacup, Preston, Lancaster, Penrith, Ilkley, Leicester, Stourbridge, Lichfield, and Darleston.

Although very many thousands of people have probably been affected, yet it is impossible to say how many, and equally impossible to give the number of deaths. For the epidemic had been in existence for nearly six months before anything except alcohol was suspected as the cause; many cases were treated as rheumatism, others as gastritis or diarrhœa, large numbers simply for the skin eruptions, and many merely as cases of chronic alcoholism. Some patients only had slight symptoms, and did not have medical attention, while in others the cardiac and hepatic symptoms were the important features.

But some idea may be obtained from certain statistics obtained by Dr. J. Niven, Medical Officer of Health of Manchester, and Mr. Tattersall, Medical Officer of Health of Salford. The former, in response to a circular received information from ninety practitioners, and came to the conclusion that there had been up to the end of November in Manchester only at least 2000 cases. Investigating his death tables and including deaths certified as due to neuritis, alcoholism, or cirrhosis of the liver, for the first ten months of the years 1897, 1898, 1899, and 1900, he found them to amount to 172, 141, 188, and 253 respectively. In Salford, Mr. Tattersall found that

[1] 'Brit. Med. Journ.,' December 1st, 1900.

in the four months from the end of July to the end of November, 1900, there were forty-one cases of death certified as due to neuritis, and twenty-five as due to alcoholism; this total of sixty-six contrasted with twenty-two in the first seven months of the year, thirty-nine in the whole of 1899, thirty-one in 1898, and twenty-seven in 1897.

Symptomatology.

1. *Complaint of patient.*—In answer to the usual question, "What is the matter with you?" the patients have complained of one or more of the following symptoms:—pains in the feet, hands, and limbs, burning in the soles of the feet, tingling, and "pins and needles" in the fingers and toes, shooting neuralgic pains in the trunk and limbs, difficulty of walking, weakness in the hands and legs, rashes on the body, frontal headache, running of the eyes and nose (cold in the head), bronchitis and hoarseness, a "tired-out" feeling, shortness of breath, swelling of the feet, vomiting, and diarrhœa.

2. *Aspect.*—The aspect of most of the patients is so typical that their cases can generally be diagnosed at sight, not only as they come into the out-patient room, or lie in bed, but as they walk about the streets of the city. The face is puffy, especially about the eyelids. The eyes are suffused and watery, and sometimes running with tears; in some cases the conjunctivæ being œdematous, and the vessels so congested that at first sight there appear to be subconjunctival hæmorrhages. The colour of the face varies from crimson to a dusky red, or even a copper colour. The voice is often "husky," sometimes intensely so, and the walk is that of a patient with very sore feet, so that they seem afraid to put the foot to the ground; or it is somewhat unsteady; or else there is the "high-stepping" gait from paralysis of the dorsal flexors of the ankle. In many cases the gait can be diagnosed merely by the noise of the footfall on the ground—the

"double-rap" step as I call it,—the heel coming down first, quickly followed by a sudden (not gradual as in health) descent of the anterior part of the foot, and so making the second rap. The patients very frequently are found to be rubbing the fingers together because of the numbness and tingling.

3. *The skin lesions.*—These are very numerous, and almost invariably present in some form or another in greater or lesser degree. (*a*) Erythromelalgia.—This condition, described as "painful red neuralgia of the extremities" by Weir Mitchell, or "acrodynia" by older observers, was one of the commonest lesions. The soles of the feet are crimson, as if stained with red ink, sometimes the whole surface, but more generally only where the surface touches the ground, so that there is left a normal appearance on the inner side at the hollow of the foot, and also a transverse line just beyond the distal extremities of the metatarsal bones. The sole and often the whole foot is bathed in perspiration, which may be stinking (but this is rare). The skin is also puffy, even if no true dropsy is present. On the palm the redness may, again, be uniform; but, again, more frequently it is most marked on the thenar and hypothenar eminences, and on the palmar surfaces of the terminal phalanges, the centre of the palm being normal in colour; the whole palm is wet, and may be actually pouring with sweat. Both soles and palms are tingling and burning hot, and painful, and these signs are greatly intensified by heat, so that the patient cannot sleep unless the feet are exposed to the air outside the bed-clothes.[1] The pressure of the bed-clothes cannot be borne, and the surfaces are exquisitely painful on pressure, so that, as I have said, the gait is affected, and the patients cannot use the hands even if no paralysis is present. This erythema does not become pigmented, but passes on to keratosis. (*b*) Keratosis.—This condition seems to be a somewhat late mani-

[1] Rarely the patient says his feet are very cold, but on examination they are proved to be hot.

festation, and is, at any rate, very frequently secondary to the erythema and hyperidrosis of the palms and of the soles. I have watched it develop on the hands and feet, and can thus speak with some certainty. It may take several forms; it may be in a few isolated scaly masses, either thin or very heaped up in marked prominences, and in this way previous corns on the feet, or patches of tylosis on the soles or palms become extraordinarily prominent. In some cases the keratomatous patches appear on the dorsum of the hand, between the webs of the fingers, and on the knuckles. In more marked cases, either the whole palm or sole is thickly covered with large white or dirty grey scales, which are constantly being shed into the bed-clothes; or the centre of the palm and inner side of the sole may be merely erythematous and dry, but not covered by scales. Sometimes the keratosis extends up to the ankles and on to the wrists, but the scales are now not thick, but more like a brawny desquamation. The palms and soles may both be affected, but the soles are almost always the worst, and sometimes are affected alone. Moreover, in cases where there is no pigmentation, keratosis may be present, and forms a most valuable aid in the diagnosis of a case which might otherwise appear to be merely one of alcoholic paralysis. The process is very slow (many weeks) in its development, and seems to be, if untreated, extremely chronic. (*c*) Erythemata.—These are very varied in character, and are often accompanied by great irritation. There is sometimes a scarlatiniform eruption on the upper part of the chest spreading to the neck and face, sometimes on the forearms and rest of the body. At other times, and perhaps more frequently, it is a morbilliform rash on the trunk and limbs, running into scarlatiniform patches; often it is a more distinctly papular erythema, and not unfrequently there is an acute urticaria. In some the change is so intense that there is a vesicular eruption, in which the lesions may vary in size from that of a pin's head to large bullæ several inches in diameter. Those I have seen have been almost always on the limbs.

In one or two cases the appearance has been that of a true pemphigus, and when the contents have been shed circular marks have remained, like very superficial scars. These vesicular eruptions are probably a late form of rash, even coming on six weeks after the last glass of beer has been taken. The erythematous papules sometimes become larger, run together, and are covered with scabs in patches, so that there may be after many weeks an appearance somewhat like lupus, or even of syphilitic superficial ulcerations. (*d*) Pigmentation.—This is generally not present in light-complexioned patients, or merely amounts to a darkening of pre-existing freckles. In darker people it is practically always present in greater or less degree, but in many is so diffuse that it may entirely escape notice. In most of the cases it follows on (after many weeks) the erythematous blush, which gradually turns from red to copper-colour, then to bronze, and in severe cases almost to black, so that many of the cases resemble mulattoes. Even if it is thus almost universal, it does not affect the palms and soles, nor as a rule does it touch old scars in which the deeper layers of the skin have been destroyed; but round the edge of the scar it is much intensified, the scar thus seeming of an especially white character. Round the neck, in the armpits, round the nipples, on the abdomen, round the genitals, and on the buttocks, where there has been pressure, as round the waist, or under the garters, it is much deeper in tint, and indeed resembles the pigmentation of Addison's disease; but I have not seen any pigmentation of the mucous membrane of the mouth. Although well seen on the face of many patients, yet on the whole it is more marked on the trunk. Frequently the pigmentation shows well-marked lighter spots, like "rain drops." In other cases the pigmentatation is seen on close examination to be punctiform. In others it is in isolated spots varying in size from a pin head to patches equal in size to the palm of the hand, clear light-coloured skin intervening, and often these isolated patches run together to form a con-

tinuous pigmentation. Not only is the colour like that of a mulatto, but the texture of the skin takes on the same beautifully soft velvety feel to the touch, quite different from that of normal English skin. In many cases, after many weeks a branny desquamation of the pigmented skin takes place, so that by friction one can rub off the pigmentation, as it were, and leave healthy skin underneath. Having watched numbers of these cases for weeks, I am convinced that there is a distinct sequence of events, namely an erythema followed by pigmentation, and then a desquamation, so that the pigment is really a part of the general altered nutrition of the skin and is not due to a deposit of metallic arsenic in the skin, as was once thought; this view does not necessarily exclude the idea that the drug may be partly eliminated by the skin.

(*e*) Herpes zoster.—This was the tell-tale eruption which, as I have said, gave me the key to the puzzle. When it occurred without any other very definite symptoms, then I considered I was dealing with epidemic specific herpes, but when I found other signs of arsenic poisoning present, there could be no doubt that it was also arsenical in origin. Since the discovery of the arsenic, practically every case of herpes zoster has been found to have other unmistakable signs of arsenic poisoning in greater or less degree. I have seen rarely herpes of the fifth cranial nerve, a few cases of the ascending branches of the cervical plexus, several of the other cervical nerves, many of the dorsal nerves, and one of the first lumbar nerve. In no case has the herpes been bilateral, and generally only one nerve-root was affected; but in two cases I have seen two succeeding nerve-roots affected; I have seen no herpes below the elbow or below the knee. From the great number of cases seen in this district, there is to my mind no longer any doubt that arsenic causes herpes by a direct action on the posterior spinal ganglion, just as much as it acts directly on the motor and sensory nerve-fibres. This seems to me to be a much more probable view than that put forward by Dr. H. Head, that

arsenic is only a remote cause of herpes, inasmuch as it renders a person more liable to attack by specific herpes. In fact how many of the epidemics of so-called specific herpes (such as that described by Dr. Head as occurring in 1897, during the long drought that lasted from July to November) have not really been due to arsenical poisoning? From actual therapeutical observation, I have seen a few cases of herpes develop when I have been giving small doses of arsenic in which the only other sign of arsenical poisoning was lachrymation and a silvery tongue. I am, indeed convinced, that it may come on with quite small doses. The herpetic eruptions have always been preceded and accompanied by very severe neuralgic pains along the course of the nerve or nerves affected. And I may here state that I have had many cases with severe neuralgic pains in the arms or round one side of the trunk which I expected would be followed by herpes, but none appeared. (*f*) Nails.—In many cases the nails are affected. After the patients have stopped taking the beer for some weeks the best appearances are seen, for then there is a transverse white ridge across the nail; proximal to this the nail is normal, but distal to it the nail is whiter, cracked, thin, and towards the tip almost papery and much flattened. In some cases there have been a series of parallel transverse ridges of the nails, also suggesting a series of week-end "drinking bouts." These deformed nails of course break easily. (*g*) Loss of hair.—One or two women have told me that they have lost the hair during the attack, but this has certainly not been a marked feature.

4. *Nervous system.*—(*a*) Sensory affections have been present in practically all the cases. In the mildest they have merely consisted of paræsthesia and tinglings, and burning and pricking sensations in the fingers and toes; in others this has been combined with numbness of the hands and feet, and sometimes of the legs below the knees. I have not seen a case of *total* loss of sensation, although the numbness has been very pronounced. Part

of the apparent loss of power in the hands and feet has been due to this partial loss of sensation. In one case there was very marked, but not total, anæsthesia of the whole left fifth cranial nerve, but its motor fibres were unaffected. This is the only instance in which I have seen any affection, either sensory or motor, of the cranial nerves. Neuralgia of the arms or trunk, either followed or not by herpes, I have already alluded to. Finally, and of the greatest diagnostic importance, there was in a large number of the cases (but only if there was some loss of power) tenderness on pressure of the muscular masses of the legs and arms; sometimes deep pressure was required, but in other cases light pressure produced most exquisite pain, and caused the patients to scream out, and to exhibit a very typical facial expression of terror, or in less marked cases merely a screwing up of the facial muscles in a "grin of pain." (*b*) Motor: These symptoms were similar to those ordinarily found in so-called alcoholic neuritis. They were present in greater or less degree in about 70 per cent. of the cases. In the slighter cases there was only slight loss of grip and slight affection of the gait, and there was then no appreciable atrophy of the muscles. In more marked cases there was a total paralysis of the affected muscles, with very marked atrophy. The small muscles of the hands, especially the interossei; the muscles of the forearms, especially the extensors; and in severe cases all the muscles of the arm were involved. If the muscles of the upper arm were not affected, then also the supinator longus escaped to a large extent, as in lead poisoning. In the early stages in the feet there was loss of power with some slight irritation of the extensors of the toes, so that the great toe was well extended and "cocked up." In this stage the knee-jerk was always either present or exaggerated, but there was never any ankle clonus. But soon the muscles became paralysed and atrophied; first the interossei and the anterior tibial and peroneal groups, so that the toes were flexed, and the whole foot dropped

at the ankle into a position of talipes equino-varus. The calf muscles were next affected, and at about the same time those of the thigh, accompanied, of course, with rapid wasting and loss of the knee-jerks. The superficial reflexes were normal or exaggerated. Even in this stage the muscles on the front of the trunk were weak, so that the patients could not raise themselves in bed, and in some advanced cases there was well-marked diaphragmatic paralysis, with laboured breathing and a markedly ineffective power to cough. In one case, with comparatively slight loss of power in the limbs, the diaphragm was entirely paralysed. It goes without saying that in the most advanced cases the patients lay in bed totally helpless. There was no paralysis of the sphincters, except in the most marked cases, in which some of the incontinence was possibly due to the mental condition, and the intercostal muscles were never paralysed. I never saw any paralysis of the cranial nerves in any case. The walk I have already described as the "stepping" gait, but many of the patients were distinctly incoordinate in their movements, and swayed slightly on standing with the eyes closed, but to my mind there was never any real resemblance to the ataxic walk of a case of tabes. (*c*) Mental: In many of the cases of advanced paralysis there was the peculiar mental condition commonly found in alcoholic paralysis. This has been called confusional insanity, but it is more accurately described as a total loss of memory of time and then of place. There is a loss of initiation of ideas, but any suggestion, however absurd, is at once accepted. Thus a totally paralysed patient, who has been in bed for weeks, when asked if he has not been for a walk this morning, will say that he has, and will tell you with much circumstance where he has been; and when asked about yesterday, will perhaps say, with a little prompting, that he has been to the seaside. If asked when he came into hospital, he will always turn towards the nurse at the other side of the bed and say, "Let me see, I think it was

yesterday [or some other near date], wasn't it, nurse ?" But taking only the paralysed cases, I am inclined to think that the amount of mental confusion has been distinctly less than I should have expected from as many cases of ordinary alcoholic paralysis, which rather leads me to think that arsenic has not much effect on the cerebral cortex.

5. *Circulatory system.*—In the majority of the patients there has been some heart failure. In the milder cases this has been limited to dyspnœa on slight exertion, palpitations, post-sternal or epigastric pain, and a low tension pulse. In more marked cases the heart muscle has shown great failure, and the left side of the heart has been dilated, the apex beat has been in or outside the nipple-line and the left border not infrequently outside the nipple-line; the beat was sometimes diffuse. On auscultation the heart-sounds have approached the fœtal "tic-tac" type, the second sound being accentuated, and the diastole shortened to the length of the systole; in some cases there was a soft systolic mitral murmur. Exertion has increased the pulse rate considerably, and there has sometimes been a rapid heart without accompanying fever. So great has been the cardiac muscle failure that several patients have fainted on getting up for the first time, and undoubtedly the principal cause of death has been cardiac failure; this has been noticed as the chief cause of death in arsenical poisoning by Brouardel in the Havre epidemic in 1888 (homicidal poisoning). Œdema affecting merely the feet only or almost the whole body has been observed in 25 per cent. of the cases. On the trunk it may manifest itself by the skin taking and retaining the impression of the stethoscope over the heart. There is often a well-marked pad of œdema over the sacrum, and the genitals are sometimes enormously œdematous. The legs may have such a tense hard œdema that it is difficult to make an impression on them with the finger. There has been a fair amount of ascites, but no great amount of peri-

cardial or pleuritic effusion, certainly not so much as is said to occur in beri-beri. In the Chester cases there seems to have been an unusual amount of heart failure and œdema. Both from the cases which I have seen and from those reported in other epidemics I have no doubt that arsenic will seriously affect the heart muscle quite independently of alcohol.

6. *Respiration.*—Just as the skin is irritated by the arsenic so the respiratory mucous membrane seems to be in its whole course. There are in the early stage running from the eyes and nose, congestion of the fauces; a very marked congestion and thickening of the vocal cords producing the typical hoarse or husky voice (not due to any paralysis, as I have proved by laryngoscopic examination) and very pronounced bronchitis. Not infrequently there has been hæmoptysis in patients who were certainly not suffering from phthisis. Not a few of my cases have shown signs of phthisis with fairly rapid breaking down of the lung tissue. And it is interesting to note at the present time, when arsenic is being largely recommended for the treatment of phthisis, that some of our patients with signs of rapid phthisis give a history of apparently previous phthisis which has seemed to be in abeyance but has been lighted up in a virulent form by drinking the arsenicated beer.

7. *Digestive system.*—In many of the cases digestive troubles were the first signs; although loss of appetite was present in severe gastric cases, on the contrary in mild cases the appetite seems to have been definitely increased. There was, of course, no blue line on the gums in any case, but in a few the gums were red and softened. The tongue in the early stage had a typical thin white silvery coat, as if it had been brushed over with lunar caustic. In later severe stages it was brown, but as a rule it was moist. Vomiting quite sudden and very copious was a marked feature, sometimes occurring immediately after each pint of beer taken, or immediately after a meal. Many patients came to the hospital suffering from

sensory disturbances and said that they were spirit drinkers only, but on inquiry I found that they had been beer-drinkers a few weeks previously, but had voluntarily stopped the beer because it was not "agreeing" with them, as they were so sick; and this occurred before it was known that arsenic was present in the beer. Some cases complained of diarrhœa, and as these cases occurred in October and November, I was quite at a loss to explain the cause, especially as they had not as yet other signs of arsenical poisoning, although they were obviously alcoholics. In a few cases there has been passing of blood by the stool, but whether this was secondary to congestion of the liver or to ulceration of the intestine I cannot say. At the workhouse hospital during the last six months we have had quite an unusual number of cases of cirrhosis of the liver (this organ being much enlarged, hard, and tender) with great ascites. Dr. Sturrock, the resident medical officer at the Manchester Royal Infirmary, has noticed the same increase there.[1] Brouardel has also mentioned cirrhosis of the liver in pure cases of arsenical poisoning, and I cannot doubt but that arsenic will set up an interstitial hepatitis.

8. *Urine.*—In a considerable number of cases there has been a trace of albumin in the urine, but quite possibly this has been secondary to the cardiac failure. In many cases this disappears later on, so that I have no evidence to prove that there has been renal cirrhosis. We have not found any sugar in the urine. But a more interesting and important fact is the presence of arsenic in the urine of those patients who had been drinking quite recently. Professor Dixon Mann, on November 26th, obtained the arsenical reactions quite easily from only six ounces of urine passed by a woman who had been recently drinking, and its presence in the urine has also been detected by Dr. J. H. Abram and Dr. Nathan Raw[2] and others. There is no doubt, also, that the arsenic is excreted by

[1] 'Brit. Med. Journ.,' December 22nd, 1900, p. 1815.

[2] Ibid., December 8th, p. 1683.

the milk, as I was informed by a mother who was affected that her suckling child vomited after each meal (which had never been the case with any of her previous children); Dr. Taylor, of Salford,[1] reports also a clear case of the suckling infant being affected.

9. *Temperature.*—In the early stages in several cases the temperature has been raised, varying from 101° or 102° F. in the morning, to 102° to 103° in the evening, the other signs of early arsenical poisoning being fairly acute. In some cases this pyrexia has disappeared after a week or ten days in bed; in other cases it has lasted two or three weeks, and in a few has continued until death. Thus in the early stages in previous epidemics there has been some excuse for the cases having been diagnosed as influenza or even as typhoid fever.

Summary of symptoms and order of sequence.—From the above account it is clear that arsenic is almost certainly a cumulative poison, although some authors say that it is not so. Moveover, it is a poison which affects both the skin and the respiratory and digestive mucous membranes, the nerve-trunks, both sensory and motor, the muscles, including the heart-muscle, and the liver. As regards the sequence of the symptoms, Brouardel[2] has clearly laid them down, and I can confirm his statements; the sequence is—(1) digestive symptoms; (2) laryngeal catarrh, bronchitis, and acute skin symptoms; (3) disturbances of sensibility; and (4) motor paralysis (and pigmentation and keratosis). Widal, in the 'Hyères Epidemic,' gives the following actual dates in one of his cases:—February 8th, gastric disturbance and diarrhœa; March 4th, acute cutaneous eruptions, spasmodic cough, running of the eyes and nose; March 31st, sensory disturbances in the limbs; then, some days later, paresis of the upper and lower limbs. Health was only restored after one year.

The course of the disease is a slow one, the gastric

[1] 'Medical Press and Circular,' December 5th, 1900, p. 585.

[2] 'Annales d'Hygiène,' 1889, p. 479.

coryzal and laryngo-bronchial symptoms pass off first, then the acute skin lesions, which pass on to the chronic skin lesions, which I think will be found to last many months. The erythromelalgia and sensory symptoms are still almost as marked as ever in patients whom we have had under observation for four or five months, and judging from analogy of so-called alcoholic paralysis, the motor disturbances will last for from eighteen months to two years before they entirely disappear.

Mode of death.—In most of the cases this seems to be from cardiac failure, either quite suddenly or gradually. Some patients have died from paralysis of the diaphragm, with secondary broncho-pneumonia, and in one case at least phthisis contributed to the fatal issue.

Classification of cases.—The cases may be roughly divided into groups:—(1) Those with all symptoms fairly well marked; (2) those with skin lesions principally; (3) those with cardiac and hepatic lesions principally; and (4) those with paralytic lesions principally.

A careful examination into the history and present state of any case will, however, reveal some concurrent symptoms quite characteristic of arsenical poisoning. Thus, in a fair-complexioned woman who had no apparent symptoms but paralysis, which could not be diagnosed from so-called alcoholic paralysis, there was in addition keratosis of the soles of the feet.

Diagnosis.—Once the possibility of arsenic poisoning is recognised, there is no difficulty whatever in diagnosis. There is no other disease which will produce the same grouping of symptoms. In the early stages it is possible to mistake the condition for measles or scarlet fever, and in the later for Addison's disease, and in some cases it will be difficult in the present state of our knowledge to say that certain cases cannot be entirely explained by chronic alcoholism. Only a thorough consideration of the history, and full examination of the patient, will prevent mistakes being made. In beri-beri there are said to be but few skin lesions.

Treatment.—I shall say little on this point, for having entirely stopped the intake of the poison, the treatment becomes merely a matter of dealing with symptoms. One point, however, is of great importance; on account of the alarming heart symptoms from muscle failure no depressing drugs should be given. We must thus avoid potassium iodide, sodium salicylate, antipyrin, exalgin, phenacetin, etc. Small doses of digitalis, with some other diuretic, tonic doses of strychnine, gastric sedatives, carbonate of ammonia and senega will probably be required. For the pains we must have recourse to small doses of morphia. The burning sensation in the hands and feet is much relieved by spirit lotion. The other skin lesions must be dealt with *secundum artem*, but this is a subject which I would rather leave to the dermatologists. The treatment of the neuritis does not differ from that which is already well known.

Previous epidemics.—Space will not allow me to do more than mention some previous epidemics of arsenic poisoning. Graves[1] mentions that he had witnessed part of the curious "épidémie de Paris," which occurred in 1828, in which there were peripheral neuritis, acrodynia, and many other of the symptoms which I have above described. There can be little doubt that this was an epidemic of arsenic poisoning. I have been unable to find Chomel's original paper, but Barthélemy[2] says, also, that it appears to have been due to arsenic, and that in four or five months it caused the deaths of 40,000 persons on the western bank of the Seine, near Paris. Brouardel and Pouchet[3] call attention to an epidemic affecting nearly 500 persons at Hyères in 1888, and reported by Widal, in which white arsenic had by mistake been put into wine instead of gypsum; also an epidemic at Havre in 1888, in which fifteen persons were affected from arsenic

[1] "Clinical Lecture,' 'New Sydenham Society's Transactions,' vol. i, 1881, p. 578.

[2] Nielson's article in 'New Sydenham Society's Transactions,' vol. clxx, p. 237.

[3] 'Annales d'Hygiène,' 1889, vol. xxii.

put intentionally into food. Brouardel also alludes in passing to an epidemic which he had investigated from arsenic in bread,[1] and I have seen a statement made, but cannot confirm it, that in 1884, in the Départemente du Midi (France) some wine sold was found to contain a considerable quantity of arsenic, which was derived from the sulphuric acid with which the old wine barrels had been repeatedly washed, whereas the same wine which had been stored in new barrels was quite free from the poison.

Pathological anatomy.—This subject I do not intend to allude to, as it is being investigated by others. In the few cases in which I have been present at the post-mortem examinations, the only prominent signs were the interstitial hepatitis and the dilated flabby heart.

Personal statistics.—During the three months—October, November, and December, 1900—I had charge at the Manchester Workhouse Infirmary of 343 patients suffering from arsenical poisoning, 192 being men and 151 women. During November and December, at the Manchester Royal Infirmary (out-patient department), I treated 157 patients similarly affected, 99 being men and 58 women. This gives a total of 500 cases, 291 being men and 209 women. This preponderance of men over women is contrary to what I supposed at first was the case, but the symptoms were on the whole more pronounced in women. The deaths were thirteen, five of men and eight of women. The ages varied from twenty-six years to seventy years, and either beer or porter was invariably taken as a beverage alone or together with spirits. The amount taken has varied from as small a quantity as two pints (possibly only one and a half pints) to sixteen pints a day. The herpes was more common in men, for out of a total of twenty-one cases seen in three months, sixteen were in men. The heart symptoms with anasarca, and the liver enlargement and cirrhosis with ascites, were also more common in men. But the gastro-intestinal, the

[1] At St. Denis, where 250 were affected.

coryzal, and the sensory and motor disturbances were more common in women, and as a rule were shown in a much more marked degree. In eighty cases in which specially careful notes were taken, seven women out of thirty-seven had marked loss of memory of time and place, but only one man out of forty-three was thus affected. Also of these thirty-seven women twenty-seven were suffering from loss of power, ten of them to such a degree that movement of the much atrophied limbs was practically impossible. Of the forty-three men seventeen had loss of power, the loss being of a total character (in the limbs) in six cases. In all the cases of paralysis the legs were more affected than were the arms.

DISCUSSION.

Sir WILLIAM GOWERS (who could not be present, wrote as follows).—I regret that another engagement prevents my presence to-night. In connection with the subject of Dr. Reynolds' paper, it is curious to note the immunity from arsenical neuritis among those who take bromide regularly for epilepsy, and are obliged to take arsenic with it as the only means of preventing bromide rash. It is usually necessary to give at least 10 minims of Liq. arsenicalis to 60 grains of bromide to prevent acne, and many patients need 15 minims. Ten minims is equal to ·1 grain of arsenious acid. Out of a very large number of cases of epilepsy who have taken arsenic thus for years I only remember one case of arsenical neuritis. This is the more remarkable because the characteristic pigmentation is not at all uncommon, and is often intense. It sometimes causes much concern until its nature is explained, and I have often had to put before the patient the alternative choice—the bromide rash or the darkening of the skin. The latter has always been chosen without hesitation. The smallest quantity which I have known give rise to pronounced pigmentation was equivalent to about 100 grains of arsenious acid, taken during two years, of course in the form of Liq. arsenicalis. This freedom from neuritis strongly suggests the co-operation of alcohol in its production in beer drinkers. Two cases of arsenical neuritis which I have seen deserve mention. In one, which was most severe and characteristic, the arsenic had probably been absorbed chiefly by the lungs. The patient was a lady who had amused herself for years in working on æsthetic muslins, and had even slept on them at night. They were found on analysis to contain a large quantity of arsenic. The other was a man who presented symptoms closely resembling locomotor ataxy. I could not examine him thoroughly when I saw him first, and prescribed some arsenic. A month later I saw him again, and stripped him to test sensation. To my surprise and consternation his trunk was covered with characteristic arsenical pigmentation. On inquiry, I found he had been taking for at least a year a tonic pill of nux vomica and arsenic. I could not ascertain the exact amount. Under different treatment he entirely recovered; but for a long time his progress was slow.

DR. BUZZARD.—I have listened to the paper which has just been read with great interest. We must all feel that it furnishes a very remarkable addition to our knowledge concerning arsenical poisoning. There are three things I should like to

say at once with regard to it: (1) I have no doubt that the cases described belong to the group of what are called multiple peripheral neuritis. (2) I have no doubt that these cases are due, at any rate in considerable part, to the effects of arsenic, though I agree with Sir William Gowers that the influence of alchohol also cannot be excluded. (3) We cannot fail to appreciate the interesting and clever deduction that Dr. Reynolds made in tracing this epidemic to its source.

There is one point about which I feel a little doubtful whether I understood the author correctly. It appeared to me that he was greatly inclined to think that what we call alcoholic neuritis is really a form of arsenical poisoning. If this be so, and I have not mistaken him, I am prepared to join issue with him at once. I remember that in the first case of alcoholic paralysis that especially attracted my attention thirty years ago, which was that of a lady suffering from what would now be recognised as a typical attack of alcoholic neuritis, the disease was distinctly due to drinking brandy, and nothing else. My experience, indeed, has been that it is due especially to spirit drinking, In the early days of my observation of the disease its occurrence struck me as notably frequent among females of good social position, and it was always spirit that they drank—brandy in those days, just as it has been whisky more recently. The lady who drinks, drinks spirit of some kind, and the stronger wines—not beer. For some time indeed I thought it was exclusively among spirit drinkers that these cases of neuritis occurred, and it was only as time went on that I began to find them also in beer drinkers. The well-known Dr. Lettsom in a pamphlet published by him in 1789, entitled "A History of some of the Effects of Hard Drinking," referred exclusively to the drinking of spirits. He gave a singularly graphic picture of the condition now recognised as alcoholic paralysis, and he recognised as the cause of the disease excess in brandy and gin. He makes no reference to beer as a cause. But even supposing that beer was also taken by the inebriates described, we may be pretty sure that the manufacture of beer in those days did not include the use of the glucoses and inverts which the refinements of modern chemistry have placed in the hands of the brewer. So, also, Dr. James Jackson, of Boston, who gave an admirable account of alcoholic neuritis about thirty years later, said that it chiefly occurred among females, and was due to "ardent spirits."

The intense pain upon pressing the muscles, to which Dr. Reynolds draws special attention, is well known to be not at all peculiar to arsenical cases. It occurs in a very large majority of alcoholic cases. The keratoses I am not so familiar with, but I have seen considerable disturbance

of nutrition in the soles of the feet occasionally, though not very frequently, in alcoholic cases. I should like to ask the author some questions. Has he any idea of the proportion of cases which occurred in people who were really not excessive in their consumption of beer—who would take, for instance only two or three glasses a day? and secondly, whether in women of a suitable age he found that amenorrhœa was present, such as I have drawn attention to as occurring so generally in alcoholic cases? The comparative absence of mental symptoms appears to lend confirmation to the view that the cases were largely due to arsenic rather than to alcohol, but in some considerable number of his cases, where the quantity of beer drunk was very large, there must doubtless have been a mixture of both causes of neuritis.

Sir William Gowers has already referred to a point which I had intended to discuss, viz. that having had the opportunity of treating large numbers of epileptics he has seen many of them take considerable quantities of arsenic daily, along with bromide, for months or years, without displaying a symptom of arsenical neuritis. My experience quite confirms his in this respect. In contrast with this immunity let me refer to a report of analyses made by Mr. Kirkby of sixteen specimens of beer in connection with the epidemic, which showed the presence of arsenic in quantities varying from 0·01 gr. in one to 0·28 gr. per gallon in that which was most drugged. The average quantity contained would be about gr. $\frac{1}{9}$ per gallon, and a person consuming four glasses of such beer would take in the course of the day less than the equivalent of three minims of Fowler's solution, a quantity less by half than that which is taken for months together with impunity by many epileptics.

As a contribution to the question of toxic doses of arsenic let me mention a case which came under my observation some years ago. A male patient, aged 55, who took no alcohol, consulted me on account of symptoms which had commenced some months previously whilst taking arsenic for an hereditary chorea. Beginning with a dose of 5 minims of Fowler's solution three times a day, he had increased this by a minim in each dose every two or three days. At a dose of 13 minims he began to be nauseated, and omitted the drug for a few days, resuming it later in smaller doses, but taking on one occasion as much as 17 minims three times in the day. The administration of the drug (in less dose than this, however) was continued altogether for about fifty days, with occasional interruptions. It then ceased and was never resumed, so that when seen by me he had taken no arsenic for about eight months. He reported that towards the close of the administration of the arsenic his hands—especially the palms,—and the foot soles—especially the under surface of

the toes,—had become red and tender to the touch. There had been no darting pains to speak of, but a "prickly, pins-and-needles" sensation. Cutaneous sensibility had been much impaired, and the skin of the hands had peeled. The knee-jerks had been lost. At first, after ceasing to take the arsenic, he had improved a good deal, but recently had not advanced. During the worst of his illness his feet, he said, used to feel like clogs —so heavy that he could scarcely walk, and this feeling still—eight months later—remained, though not to the same extent. His knee-jerks, when I saw him, required reinforcement. Touches on the fingers still gave rise to "prickly feelings." He was still clumsy with his fingers, but had regained the power—which he had lost—of writing. There was still impaired cutaneous sensibility in the fingers and feet. He appeared to be gradually but very slowly recovering.

I calculate—though this is only an approximate estimate—that the whole quantity of arsenious acid taken may possibly have approached 13 grains (probably less), but this was concentrated into a period of about fifty days. The symptoms of neuritis were marked and severe, and eight months after the use of the arsenic had been discontinued they were still evident. This contrasts with our experience of epileptic patients who will take 20 or more grains in a twelvemonth without displaying any toxic symptoms. On the other hand, in the cases described by Dr. Reynolds, it would appear as though the administration of doses far below those commonly employed therapeutically had occasioned lesions more severe than those which occurred in the case I have mentioned. This curious anomaly stands in need of explanation.

Adjourned Discussion, February 12th, 1901.

Dr. Ormerod said:—It is my duty, having moved the adjournment of this debate, to reopen it to-night. But I only do this formally, for seeing that we have here many eminent gentlemen from the North who have been actual witnesses of this outbreak, and that, owing to the sad circumstances which prevented our debate a fortnight ago, they are here for the second time to-night, I prefer at once to make way for them.

Dr. Dixon Mann (Manchester).—You have had the clinical aspect of this outbreak well put before you by Dr. Reynolds and others, and I do not purpose going over the same ground. I will, however, say a word or two with regard to an unusual type of arsenical poisoning, of which I have seen a few cases during this outbreak. This type is peculiar, because it may occur without any of the ordinary symptoms associated with

chronic arsenical poisoning, *i. e.* without neuritis, and without any skin manifestations. In this form, of which there is more than one variety, you have a temperature varying from one to three degrees above normal; you have possibly sweating, which may be excessive, or may be hardly noticeable; you have a mental condition in which the patient is apathetic and even somnolent; if roused there is a little tendency to ramble. In two cases this mental condition was replaced by a state of mental irritability suggestive of cortical irritation. The chief indication is a singularly weak action of the heart, with dilatation and a tendency to œdema or to hyperæmia of the lungs. The patient makes no complaint; there is no pain, but he simply lies in this condition, which continues from one to several weeks. If recovery takes place it is very gradual; if the patient dies, death usually occurs rather abruptly from heart failure, which has been menacing all along. This form has been mistaken more than once for enteric fever, though there are no bowel symptoms, no enlargement of the spleen, in fact, nothing characteristic of enterica. In another peculiar form of chronic arsenical poisoning you have, or may have, absence of the usual signs of neuritis; there is no temperature, but from the first there is a condition approaching collapse, associated with diarrhœa and sometimes vomiting, very weak action of the heart, and throughout a tendency to heart failure. Of course this closely resembles the ordinary subacute form of arsenical poisoning; but it presented this peculiarity, that the symptoms did not come in one case until four and in another until seven days after the patient had ceased drinking arsenicated beer, so that it cannot be regarded as of the ordinary subacute type.

I will now pass on to the chemical side of the question. With regard to the elimination of arsenic, we have always looked upon it as a non-cumulative poison. Of course the term is relative, but we have always understood that arsenic does not remain locked up in the tissues. Now, taking the channels of elimination, we may divide them into primary and secondary, the primary being the kidneys and bowels. Years ago I showed that it was very easy to detect arsenic in the urine within half an hour of the administration of five drops of Fowler's solution; and further, from the same dose, arsenic may be detected in the first motion subsequently passed; so that the elimination commences very promptly, and under ordinary circumstances it is continuous. In acute arsenical poisoning I shall not be very far off the mark if I say that arsenic has not been found in the urine longer than from eight to ten days, that is to say, after a single dose. In chronic poisoning we have a different state of things, and frankly I was not prepared for what I found in the course of these investigations. It would appear, when repeated small

doses of arsenic are taken over a prolonged period, that the elimination rate is not able to keep pace with the rate of ingestion; there is consequently accumulation of the poison, which is backed up, rather than locked up, in the tissues. Now, arsenic does not combine with albumen in the same way that many of the heavy metals do. That it does not intimately combine with the living tissues is evinced by the fact that after large doses it is possible to obtain evidence of its presence in the urine by simply acidulating with hydrochloric acid and then passing sulphuretted hydrogen through it. This cannot be done with the ordinary heavy metals. Moreover, post mortem, a small portion of an organ, such as the liver, after a large dose of arsenic has been absorbed, readily gives evidence of the presence of the poison by means of Reinsch's test, without any preliminary preparation, showing that the arsenic is but loosely combined with the organic matter. Notwithstanding this, arsenic, when given repeatedly in small doses, does accumulate in the system, this possibly due to defective elimination. I have obtained arsenic from the urine as late as the twenty-sixth and thirty-first day after the patient had ceased taking the arsenicated beer. To put the matter beyond doubt, I may mention that I only cite hospital cases under my own care in the wards. The results of analyses of the viscera show that time is not the only factor in the elimination of arsenic from the system. I made seven investigations on behalf of the coroners of Manchester and of Salford, all the seven being women. One of these cases was in the hospital at Crumpsall for twenty-three days, and I found no arsenic in the viscera. In another, which was in hospital for fifty-two days, I found a small amount of arsenic in the liver, spleen, and kidney. Turning to the cases which did not die in hospital, I do not rely so much on the statements as to the alleged periods of abstention from beer before death. In one patient who had taken no beer for six days there was a small amount of arsenic in the liver, spleen, and kidneys. In another, described as a moderate drinker, who had had no beer for three weeks, I found an eightieth of a grain in the liver, and a perceptible amount in the kidney, spleen, and a trace in the stomach. In another, also without beer for three weeks, I found the equivalent of a thirtieth of grain in the liver, as well as a perceptible amount in the kidney and spleen, but not in the small portion of brain which I received.

Coming back to the question of elimination, the chief secondary channels are the skin and its appendages. Although I knew, of course, that arsenic was found in the skin in cases of chronic poisoning, I was not at all prepared for the large amount that is present. The keratosis that occurs offers very ample opportunity for making observations of this kind, and I have obtained a

number of specimens from different subjects, and found that in the majority of these cases very large proportions of arsenic were present. In one case I got eight tenths of a milligramme of arsenic from ten grammes of the horny, epithelial scales. In another, from three grains of horny scales, I obtained large crystals of arsenious acid. The large amount of arsenic so eliminated by the human skin is rather suggestive; and I could not help thinking that it might have something to do with the well-known efficacy of arsenic in diseases of the skin, many of which are microbic; the amount of arsenic present in the skin, after prolonged arsenical treatment, being sufficient to inhibit the multiplication of micro-organisms. In hay fever, also, the quantity of arsenic eliminated by the mucous membrane after medicinal doses may act in the same way. The arsenic in the horny scales is evidently only partially combined, some of it being soluble. By boiling three grains of the scales in distilled water for five minutes, and filtering, I obtained crystals of arsenious acid from the filtrate. Then, again, from a tenth of a gramme (gr. $1\frac{1}{2}$) of nail cuttings, I got ample-sized crystals. In hair, too, a considerable amount was found. All this, of course, was known before, but arsenic was spoken of as a thing that might be found, and to insure success former investigators employed large quantities of keratin tissues, whereas small quantities will suffice. I also found that a considerable quantity of arsenic may be absorbed and eliminated without producing any obvious symptoms.

The presence of arsenic in the skin and its appendages in cases of chronic arsenical poisoning, and the ease with which it may be found, constitute a valuable aid to diagnosis after the urine has ceased to yield any evidence.

The affinity of keratin tissues for arsenic seems to me to have an important bearing, inasmuch as it may be the cause of the initial stage of the neuritis and the brain symptoms. The axis-cylinder and the white substance of Schwann are covered with a sheath of neuro-keratin, and are connected with numerous oblique and transverse fibrils. Neuro-keratin also exists in the grey and white matter of the brain; the latter contains as much as 2·5 per cent. Assuming that neuro-keratin has the same affinity for arsenic that I have shown keratin itself to possess, it is not unreasonable to suppose that this may have a determinative influence, notwithstanding the fact that multiple neuritis is mostly parenchymatous.

Dr. Judson Bury (Manchester).—This epidemic of arsenical neuritis has raised some important questions. There is the question of pigmentation; many of the cases of neuritis have shown but little pigmentation, and it is not always easy to determine whether darkening of the skin under a waist band is

due to arsenic, or is merely the result of dirt and pressure. Scaliness of the feet, too, in a form somewhat resembling that due to arsenic, is not uncommon in hospital cases where arsenic can be excluded. Then there is the important general question as to the influence of alcohol in the present epidemic. The subject of alcoholic peripheral neuritis is reopened; Dr. Reynolds has, indeed, aimed a blow at its very existence; he says that for many years he has doubted whether ethylic alcohol *per se* ever causes peripheral neuritis, and that he has never seen a genuine case of neuritis in a person who has taken whisky only. Obviously, in the future we shall have to be careful to obtain accurate information regarding the exact composition of the alcoholic beverage taken by any sufferer from peripheral neuritis. In the meantime, let us briefly consider existing evidence. I am not aware that there has ever before been a real epidemic of peripheral neuritis in Manchester. On looking through the infirmary records I find that from twenty to twenty-five cases of peripheral neuritis has been a fair average number in the hospital during a year. Last year the admissions rose to sixty-two, and these occurred mainly during the last three months, so that if the same proportion had existed throughout the year, the number of admissions would have been five or six times greater than the average. Then all over the district doctors were thoroughly aroused to the fact that there was an epidemic of neuritis. There is also the fact that sulphuric acid contaminated with arsenic was first used in the spring. With this evidence before us, there can be no doubt that arsenic, in poisonous doses, was not present in the beer that was consumed before last year. This being so, what was the cause of the twenty to twenty-five cases of so-called alcoholic neuritis that were yearly coming into hospital before the epidemic, and that may occur in the future? I presume that beer, in the future, will be free from arsenic. Does Dr. Reynolds believe that we shall have no more cases of peripheral neuritis from alcoholic beverages? Furthermore, I have seen peripheral neuritis in sailors who have taken rum, in ladies who have taken only brandy, and in other persons whose sole or chief drink has been whisky. Dr. Williamson has recently recorded a well-marked case of peripheral neuritis in a man who had taken whisky and no other form of alcoholic beverage; the whisky was analysed, and found to be free from arsenic. This case alone is enough to prove that alcoholic neuritis does occur. Now, I am unable to prove that peripheral neuritis may be caused by ethylic alcohol *per se*, but I am convinced that it occurs in spirit drinkers, and I shall continue to believe in an alcoholic form of peripheral neuritis until Dr. Reynolds or some other observer proves that it is not alcohol,

but another ingredient of the alcoholic beverage which produces neuritis. Holding this over, I may pass to a brief consideration of the diagnosis of arsenical from alcoholic neuritis. In my experience, pigmentation of the skin has not been a striking feature in the present epidemic. As a rule it has to be carefully looked for. Far more important is the erythema and the scaliness of the hands and feet. Just a word as to terminology—is it correct to call the association of erythema with pain and tenderness erythromelalgia? The latter term is usually applied to a relapsing affection, in which the redness is often limited to one foot, and affects only the lines of pressure. Now, in the cases before us the erythema is persistent, it affects both feet, and frequently involves their inner as well as their outer aspects.

With regard to the brain, although the cortical cells are doubtless in some cases attacked by arsenic, a decided mental change, with defective memory and chronic delirium, is strongly in favour of poisoning by alcohol.

Coming now to the limb phenomenon, I believe that it is impossible to exaggerate the severity of the cutaneous hyperæsthesia in arsenical neuritis. So severe is it that merely stroking the palm or the sole will cause agonising pain; perhaps its most remarkable feature is its persistence. I have a patient who has been in hospital for several months; his paralysis has almost passed away, yet cutaneous hyperæsthesia of the hands and feet is most extreme. The slightest possible squeeze of a finger or a toe, or the stroking of the soles of his feet, produces the most intense pain. Now, I do not think that hyperæsthesia of the skin is ever so marked or so persistent in alcoholic neuritis. In many arsenical cases the joints of the fingers and toes are painful and swollen; this, too, I regard as a distinction from alcoholic cases. With regard to the muscular system, if we take groups of cases we find a greater tendency in arsenical than in alcoholic neuritis—(1) to a wider distribution of paralysis; I have seen the face, the diaphragm, and the lower intercostal muscles affected in different cases; (2) to more rapid atrophy of the muscles associated with fibrillary contractions of their fibres; (3) to more rapid progress of the paralysis; thus the stages of paralysis in the hands and feet succeed one another more quickly than in alcoholic neuritis; (4) to inco-ordination of movement: ataxia is rare in alcoholic cases, it is fairly common in arsenical cases. In a type case of alcoholic paralysis the extensors of the wrist and the flexors of the ankle are predominantly affected, whereas arsenic tends to pick out and attack more severely the extensors of the fingers and toes. The arsenical foot has a peculiar hollow appearance, owing to the great increase in the instep. In the arsenical hand

the fingers are curled, and often cannot be extended, owing to contraction of the flexor tendons, the little and ring fingers being the most curled and fixed. The palmar surface of the hand, especially on the inner side, presents a close resemblance to that seen in Dupuytren's contraction.

Dr. KELYNACK (Manchester).—The clinical features of the recent outbreak of arsenical poisoning in beer-drinkers have been so fully described by previous speakers, that it is unnecessary to refer to them further, except to point out that many of the points are clearly indicated in the series of drawings, photographs, and casts which I have placed on the table. The casts are of particular interest, in that they have all been taken from patients under the care of Professor Dreschfeld, through whose kindness I am enabled to show them. Fortunately we have a few casts also of "alcoholic" cases, taken as far back as 1893, and comparison of these with the casts of hands and feet from patients with arsenical peripheral neuritis from contaminated beer shows that there is practically no difference in the muscles affected, and that the consequent deformities are similar. As regards the pathology of the condition, the effects of arsenic upon the system appear to be considerably modified by concomitant conditions. Our investigations go to show that the peculiar circumstances of the introduction of the poison have led to an increase in the rate of absorption, to exceptional accumulation in the body, and to a retardation in its elimination. We are also of opinion that the alcohol or other ingredients of alcoholic beverages have in many instances greatly accentuated the effects of the poison. A consideration of such circumstances will explain many cases where patients have only consumed very moderate quantities of beer or stout and yet suffered severely. Passing to the chemical aspect of the question, one is bound to admit there has been considerable difficulty among the analysts as to the best method of detecting arsenic in beer. Difficulties have also arisen from the fact that the acids, zinc, and other materials constantly used in testing, were found oftentimes to be greatly contaminated with arsenic. Throughout my work I have had the assistance of my friend and colleague, Mr. William Kirkby, of Owens College, and I should like to refer to his apparatus, designed to apply the Gutzeit test to the detection of arsenic in foodstuffs. It is an apparatus which, I venture to think, will prove of great assistance to chemists and toxicologists, as it greatly facilitates the ready recognition of arsenic in such compounds as beer. As to the elimination of arsenic from the body, I have seen two infants where the symptoms pointed to the elimination of arsenic in the mother's milk. In one case we obtained some of the milk, but were

unable to prove the presence of arsenic therein. We have examined a number of specimens of urine, and are able to state that there has been a continuous elimination of arsenic by the kidneys during a period of six weeks after stopping the contaminated beer. We also find arsenic to be eliminated in the desquamating cuticle, and in one patient, after five weeks' residence in hospital, we still found such a quantity present that a distinct mirror could be obtained with Marsh's test. We have formed quite a collection of hair, cuticle, and nails from these arsenical cases, and hope to have some interesting results to record in a short time. The varying quantity of arsenic in the glucose and invert sugar must be remembered when endeavouring to make clear the very difficult problem of dosage. We have had large numbers of glucose and invert sugars submitted to us, and Mr. Kirkby finds that the amount of arsenic present has varied from ·03 to ·05 per cent. It also seems that all these contaminated sugars have had an acid reaction. Then, again, as to the range of substitutes. The proportion of sugar used by different brewers to displace malt has varied very greatly. In some cases there has only been five pounds to thirty-six gallons, *i. e.* 10 per cent.; others use from 30 to 40 per cent.; and one brewer was in the habit of using 50 per cent. The glucose in this instance contained ·04 per cent. of arsenic, and the beer 1·4 grains per gallon. A large number of other bodies used in connection with making beer have been examined, but in none was arsenic found in sufficient amount to account for that found in the contaminated beers. With regard to the dosage, which to medical men is a matter of great interest and importance, one finds that the arsenic present in the beers has varied within such wide limits that it is almost impossible to ascertain the exact amount taken by any patient. For instance, if a patient drank a beer which contained ·14 grain per gallon, and took half a pint of this; that would only mean taking $\frac{1}{100}$ of a grain of arsenic at a time. Many, however, have taken quite a gallon of beer daily, and that would be something like a sixth of a grain daily. Some cases, however, have been met with taking the beer from the brewer who was using 50 per cent. of the contaminated glucose, and here the dosage was equal to 1·4 grains per gallon. The whole outbreak has raised so many problems, that time and much further research will be necessary before a complete solution can be arrived at.

Sir LAUDER BRUNTON.—I regret much that other engagements have prevented me from hearing the admirable paper by Dr. Reynolds, in which he has treated the symptoms of arsenical poisoning so very fully that I cannot add anything to them, but perhaps I may be allowed to attempt to classify them. It is to be remembered that irritant substances, especially

if applied in a concentrated form to the skin or mucous membranes, may act directly upon them and produce local irritation and inflammation. Thus mustard in the form of a sinapism may cause inflammation of the skin, or when swallowed may produce vomiting, although none of it has been absorbed into the blood. But some irritants, especially if used in a dilute form so that their local action does not interfere with their absorption, enter the blood and are carried by it to every organ and tissue in the body. They thus reach the skin and mucous membranes from the inside, and may be eliminated by them. When conveyed in this way they may produce more intense inflammation than if they were directly applied. Arsenic is an irritant which belongs to this class. When it is brought into contact with the skin by articles of clothing or by work with arsenical materials it may cause dermatitis, and when swallowed either accidentally or purposely it may produce vomiting, diarrhœa, and inflammation of the intestinal canal. But John Hunter, Sir Everard Home, and Sir Benjamin Brodie have shown that when arsenic is applied to a wound it produces more violent and more immediate inflammation of the stomach than when the poison is administered internally, and that this inflammation of the stomach precedes any appearance of inflammation in the wound ('Phil. Trans.,' 1812, pt. i, pp. 209, 210). Brodie concludes that "it may be inferred that arsenic, in whatever way it is administered, does not produce its effect even on the stomach until it is carried into the blood." This conclusion is perhaps too sweeping, and not strictly true for arsenic in large doses and in a concentrated form; but it is probably quite correct when the poison is taken in moderate or small doses and in a diluted form, as in the beer at Manchester.

The observation of Dr. Dixon Mann that symptoms of subacute poisoning have occurred one or more weeks after arsenic had ceased to be taken confirm and illustrate these experiments. In Dr. Mann's cases it would appear that in the elimination of the poison the stomach had been affected in much the same way as in Brodie's experiments. Whilst circulating in the blood arsenic is carried to every organ and tissue of the body, and affects markedly the nervous system and muscles, the mucous membranes and skin. During the process of elimination it irritates all the mucous membranes and skin and produces corresponding symptoms. By irritating the mucous membrane of the stomach it causes loss of appetite, nausea, vomiting, and epigastric pain. In the intestine it produces colicky pains and diarrhœa. By irritating the respiratory tract it gives rise to coryza, cough, hoarseness, and oppression, retro-sternal pain and bronchitis, with occasional hæmoptysis. In the eyes it causes irritation, conjunctivitis, and œdema of the eyelids. In the skin

it produces all sorts of eruptions, three of the most marked being pigmentation, herpes, and keratosis, the epidermis peeling off the palms of the hands and soles of the feet in large flakes. Keratosis is probably due to the local action of arsenic upon the skin, for Ringer and Murrell found that in frogs poisoned by it the cuticle could be readily stripped from the body, and Nunn showed that this was due to softening of the protoplasm in the epidermis, so that it became almost completely detached from the dermis. The herpetic eruptions, however, are dependent to a great extent upon the action of the drug on the nerves. Arsenic appears to cause inflammation of the sensory, motor, and trophic nerve-fibres, as well as to act upon both sensory and motor centres in the spinal cord. It is rather difficult to decide how far the nervous symptoms are of peripheral and how far they are of central origin. The sensory symptoms are probably chiefly due to peripheral irritation, and consist in tingling, numbness, pins-and-needles, with more or less pain or burning, and extraordinary sensitiveness of the feet and of the muscles, especially those of the calf. The motor weakness also appears to be chiefly due to peripheral neuritis; but if we may judge from experiments on animals the motor cells in the spinal cord are also affected, so that the peculiar ataxic gait observed in some cases may be due to a combined peripheral and central action of the arsenic. The alterations of the nails and subcutaneous œdema are probably due to a great extent to changes in the trophic nerves. The cardiac weakness is of double origin, and is caused by fatty degeneration which affects all the muscles of the body, but especially the muscle of the heart, and also by paralysis of the cardiac ganglia. The extraordinary number of cases of peripheral neuritis which have occurred in this epidemic, together with the fact that this disease has been specially observed and described by Ross and Dreschfeld in Manchester, naturally raises the question whether peripheral neuritis may not be a disease caused in most, if not in all cases, by arsenical poisoning, and whether poisoning by arsenic may not have been going on to a greater or less extent in Manchester for many years.

A good deal may be said on both sides of this question. On the one hand, it cannot be denied that peripheral neuritis may be caused by toxins, for it is found in diphtheria, where no poison except that of diphtheria has gained access to the organism, and Sidney Martin has shown that the diphtheritic toxin, apart from the bacillus, will produce neuritis in animals. It is commonly supposed that alcohol will cause the disease, but it is by no means certain that ethylic alcohol will do so, and alcoholic neuritis in spirit drinkers may possibly be due to other substances than ethylic alcohol. A remarkable observation

was communicated to me in a letter by Sir William Gairdner, who saw many cases in Manchester about sixteen years ago, although he rarely or never saw them in Glasgow, notwithstanding the large quantity of whisky which was drunk there, and which ought to have produced the disease. When I first went to Manchester to investigate the epidemic I started with the idea that symptoms of poisoning were probably due not to the arsenic in beer, but to some other impurity; but I soon found that the arsenical origin of the epidemic could be proved beyond a doubt. The present epidemic is certainly due to contamination of beer through glucose and invert sugar made by one particular firm, who had been supplied with sulphuric acid containing a very large quantity of arsenic. But the fact that arsenic has now been found both in hops and malt renders it not improbable that cases of peripheral neuritis in Manchester may for years past have been due to contamination of beer by arsenic through the hops and malt. Although it is not yet certain, it seems probable that this contamination has arisen from the use of coal or coke containing arsenic in the process of drying the malt and hops.

Another point that arises is how far these symptoms of arsenic poisoning are due to arsenic *per se*, and how much to arsenic combined or associated with other substances. The observation that some of the patients have presented symptoms of cerebral congestion or failure reminds one of the very unfortunate experience which occurred many years ago in the laboratory of Prof. Mathieson. We know that mercury of itself has no great tendency to irritate the brain, but in making experiments with mercuric ethide, where the mercury is combined with ethyl, the two assistants both suffered from poisoning, and one had mental derangement for a year and then died. Similarly it would seem that the alcohol or some other substance in the beer has tended to direct the action of the arsenic to the nervous system. The observation of Osler, referred to to-night, seems to show that arsenic can be directed to the nervous system by combination with brandy, but it seems not unlikely, from the fact that so many of the patients suffered from comparatively small doses of arsenic, that it may either have had its action specially directed to the nervous system by the alcohol or hops in the beer, or may have been actually combined with some organic substance in the beer which rendered its action more intense. In the Middle Ages it was the custom, instead of giving arsenic itself as a poison, to poison a pig with it, or to kill it and rub arsenic into it, and then to hang it up and let it drain. The droppings were said to be more poisonous than the original arsenic. It is possible, therefore, that in beer containing arsenic there is a compound more toxic than arsenic

itself. I have secured the assistance of Professor Hewitt in investigating this subject, and we hope before many months to make a report upon it. There is another question, namely, how far these symptoms are due, not to arsenic, but to another hitherto unsuspected inorganic poison, namely, selenium, present in the beer, but this will be dealt with by Dr. Tunnicliffe. We are much obliged to Dr. Reynolds for his admirable paper, and for the extreme interest attached to the paper and to the discussion which it has elicited.

Dr. LUFF.—I should like to add my meed of praise to Dr. Reynolds for his valuable and ingenious discovery. Having done this, perhaps he will permit me to say that in a certain book on Medical Jurisprudence, which shall be nameless, it is pointed out that in cases of peripheral neuritis of doubtful origin it is always advisable to test the urine for arsenic. Dr. Dixon Mann's results in respect of the elimination of arsenic are also very interesting. As he modestly says, the facts are not new, but, speaking for my own part, I may say that we previously had only a vague idea that there was a slight elimination of arsenic by the skin; but he has shown us that arsenic is excreted in very large quantities by the skin, nails, and hair. I believe that these results will eventually prove to be of very great toxicological importance. With regard to the question of the combined effects of arsenic and alcohol, I do not propose to discuss the problem raised by Sir Lauder Brunton, as to its being in combination with the ethyl group or other ethereal compounds present in the beer; but during the discussion this evening I had recalled to my mind a remarkable case of arsenical neuritis which I saw five years ago. It was the case of a man suffering from splenic anæmia, whom I was treating with arsenic in moderate doses, five or six minims of Fowler's solution three times a day, and who after a short time developed sudden and remarkable peripheral neuritis. It amazed me at the time, until I found he was a man who had been addicted to alcohol in more than moderate quantities. He had never shown signs of alcoholic neuritis, but I took it that he was perhaps on the verge of alcoholic neuritis, and that the addition of arsenic determined the event. I am rather surprised at one of the statements in the paper of Dr. Reynolds, that vomiting is a marked feature of this form of arsenical poisoning. I certainly differ from him, because, although the number of cases I saw during my visit to Manchester were, of course, small compared with the number he has seen, yet I took very careful notes of the forty cases I saw, and I found that vomiting was not a prominent symptom. Colic and vomiting had occurred in 36 per cent. of the cases only that I saw; and even when vomiting did occur it was generally in cases

where very large quantities of beer had been consumed, and I was inclined to ascribe it to the gastric catarrh caused by the consumption of those very large quantities of beer; in fact, it was to me a matter of interest that in contrast with subacute or acute arsenical poisoning, vomiting was not characteristic of this particular form of poisoning. I classified the symptoms of the forty cases, and in 91 per cent. the first signs were pains in the feet and loss of power, then tingling and pain in the calves, while pigmentation was present in 77 per cent.; so that it was a fairly constant symptom. As to whether arsenic is a cumulative poison, certainly we have never hitherto considered it to be so. I am bound to confess, however, that we must now alter our opinion, and admit that arsenic can be—I will not say locked up, but deposited in the tissues in a way not hitherto suspected. Dr. Reynolds mentioned a case where, six weeks after drinking the beer, bullæ appeared. That is to me most remarkable, and must point to the retention of arsenic in the skin for a long time, or else to its having produced certain nervous effects which were lasting.

Dr. TUNNICLIFFE.—From a consideration of the symptoms I have been led to search for other impurities than arsenic in the sulphuric acid. The rare metal selenium is known to produce in animals symptoms resembling those due to arsenic, though tolerance to its effects can never be produced. The effects of selenium on the human subject are at present unknown. In dogs, wasting, independent of digestive trouble, is a marked feature, and pigmentation also occurs. I have analysed the poisonous beer and glucose, and have proved that both contain selenium or selenious acid. This metal has never been looked for before in cases of alcoholic paralysis, and it is possible that it may play an important part, though undoubtedly in the recent epidemic arsenic has been chiefly to blame.

Dr. FREDERICK TAYLOR.—One remark in the paper attracted my attention, and I thought from the way in which it was made that it was going to have some bearing upon the other statements. This application I have not been quite able to see, still it is of importance in connection with neuritis, and I therefore refer to it. Dr. Reynolds says, "It may be at once mentioned that the only forms of peripheral neuritis associated with great muscular pressure and pain are the alcoholic, the arsenical, and that met with in beri-beri." I do not agree with that statement. I have certainly met with cases of peripheral neuritis, which appeared to be due to other causes, in which the characteristic tenderness of the calves was noticed. Of course I may have some difficulty in proving absolutely that none of these patients took alcohol in any form, or had arsenic, but there is no evidence of it that I have been able to find.

Within the last six or eight months I have had five cases of peripheral neuritis, in all of whom tenderness of the calves was present. One, it is true, was a case of poisoning by arsenic, administered for therapeutic purposes. She was a young girl, and, in reference to what has been said of the added influence of alcohol in such cases, I see no reason to suppose for a moment that in her the arsenic was associated with alcohol. Another is a case of typhoid fever in which the calves are still tender. Another was the case of a youth who had pleurisy, with some consolidation of the lung. This boy has had a very definite peripheral neuritis affecting the lower extremities, and there has been this tenderness of the calves. He has had no arsenic and no alcohol, and I attribute the neuritis to septicæmia. Another young woman, a nurse, in whom there was not the slightest suspicion of arsenic or alcohol, had a slight degree of peripheral neuritis, now rapidly improving. This is a case in which there is, so far, no evidence as to causation, and so there remains an element of doubt. But the most positive case is that of a woman, aged twenty-four, who, having had diphtheria a month previously, had a very pronounced peripheral neuritis with weakness of the extremities and of the cervical muscles, and great tenderness of the calves. Here there is not only no history of alcohol or arsenic, but she has neuritis from a recognised efficient cause, producing characteristic effects.

Dr. Sydney Ringer.—I wish to point out that any substance of the nature of a poison introduced into the body affects all the tissues, though some may suffer more than others. Take a potassium salt for example. This is a general poison and affects all the tissues, probably in an equal degree. If you poison a frog with it, he first loses voluntary movement, and next reflex action, while the nerves still conduct impressions; but ultimately the nerves follow, and then the muscles. Arsenic is also a general poison, and as with potash salts, the brain, cord, nerves, and muscles are paralysed; but its action is more specialised than is the case with potash salts, as is shown by its action on mucous membranes and on the skin, and I do not think sufficient attention has been drawn to its general action, attention having been concentrated on its effects on the nerves. It also acts on the muscles, and the heart muscle is early involved. Some of the muscular wasting is no doubt due to the direct effect of arsenic on the muscle itself.

Sir Dyce Duckworth.—In reviewing the interesting discussion which has taken place this evening, I have been impressed by the thought that my experience of the use of arsenic as a drug has furnished me with so little knowledge of the noxious

effects of this agent. I have employed it in all quantities up to half a drachm of Fowler's solution in the day, and have but rarely seen any important toxic effects. It is therefore a noteworthy fact, if fact it be, that the continued use of very small quantities should induce the grave results of which we have heard. We supposed we knew all the ordinary effects of the drug long before the fact of arsenical pigmentation was generally recognised, and that has only been the case for some ten or fifteen years. Yet no symptom is more common than this. I have now two children under my care, one fair and one dark, who are gradually developing pigmentation under courses of arsenic. One's thoughts go back to the Styrian arsenic-eaters, and to the practice of veterinary surgeons respecting the employment of the drug as a nutrient tonic especially determined to the skin; and the important contributions of Dr. Dixon Mann to the debate to-night indicate how certainly arsenic finds its way to the cutaneous system, and may remain there. My own belief in regard to the class of cases before us is, that the toxic effects are not solely attributable to the arsenical contamination, but are probably due to the combined effects of alcohol and possibly of some other agent in beer, both together acting differently from either by itself. We have an analogy in lead poisoning, where we find the noxious effects of this impregnation intensified by alcoholic abuse. Lastly, I would venture to hope that amongst the good results of this outbreak may be the brewing of a purer beer, and a more moderate consumption of it by the community.

Dr. NATHAN RAW (Liverpool).—The recent epidemic of arsenical poisoning in Liverpool does not seem to have been so extensive as in Manchester, although some of the cases have been of a severe type. During the last three years, out of 12,623 patients admitted into Mill Road Infirmary under my care, there have been 226 cases of alcoholic neuritis, of which number 147 have presented symptoms which might be attributed to arsenic. Of these 226 cases of alcoholic neuritis 51 died, the apparent cause of death being general asthenia, with cardiac failure in most of the cases. As bearing on the question as to when the arsenical contamination of beer commenced, the infirmary statistics are of great value, and recent disclosures at the inquest in Manchester have proved that my suggestion that the poisoning commenced in May last is probably correct. During the year 1898, 26 cases of alcoholic neuritis were admitted; in 1899, 34 cases; and in 1900, 143 cases; and whereas there were only 8 cases admitted up to the end of April this year, a sudden remarkable increase commenced in May, and steadily progressed up to January last. The manufacturer of the sulphuric acid supplied to the glucose firm admitted that previous

to last March he had supplied acid free from arsenic, but that after March 1st he supplied acid containing arsenic, and hence the epidemic. With regard to the cause of alcoholic neuritis, I am convinced that, from a careful observation of a large number of cases, beer and porter are the general drinks consumed, by far the greater number being due to beer alone; but I have certainly seen cases of undoubted alcoholic neuritis where the patients have only taken brandy and whisky. With regard to this point I was particularly struck with the fact that in Scotland one very rarely saw peripheral alcoholic neuritis, and it is well known that there the popular drink is whisky. I believe, also, that the serious lesions are caused by continual drinking of moderate quantities every day for prolonged periods, rather than to sudden outburst where large quantities are taken and rapidly excreted. The great majority of cases of ordinary alcoholic neuritis occur amongst women of the poorer classes, and in Liverpool it is the custom for women to congregate in each other's houses and send for cheap beer during almost the whole of the day. By consuming it off the premises they get what is called the "long pull," which means if they ask for a gill they get nearly a pint. I mention this, because when a patient says she has taken a pint of beer a day one can safely assume double that amount. As far back as last August I commenced a thorough investigation into the cause of this great increase of neuritis, and I actually settled upon the beer as the cause; but I put it down to an increase of drinking amongst the poor, probably due to the war and extra pay received for relatives. I certainly never suspected arsenic, and it was only when I read the brilliant discovery of Dr. Reynolds that the whole thing was made plain. The symptoms and appearances have been so ably and fully described by various observers that I will not refer to them here, but I would like to refer to a few points. My cases have been divided into two great classes: (1) acute; (2) chronic. In the acute cases the patients had invariably had a heavy bout of drinking beer, and in one marked case a man had been a teetotaler for three months, and then had taken forty-two pints of beer in three days, the symptoms appearing in forty-eight hours. In several of these cases there was marked pyrexia; the temperature in three cases reached 102·4°, with great pain in the left side, simulating pleurisy—probably neuritis of intercostal nerves. The eye symptoms are different from those observed in alcoholic neuritis; there is intense itching along the edges of the eyelashes, with puffiness and œdema of the lids, not the injected bleary eye of the alcoholic. I found arsenic in the urine in five cases out of thirty-three examined, but in no case was I able to find it after ten days from admission. The pigmentation appears to be of two kinds: one that desquamates freely in

large scales and is of a dirty brownish-black colour, and a general mahogany discoloration without desquamation at all, the discoloration simply clearing up. The pigmentation appears to require several weeks to develop, as none of my admissions have developed it since December 1st. I cannot bear out Dr. Reynolds's observations that the pigmentation is confined to dark people, as I have had well-marked pigmentation in quite fair women. The sensory symptoms have certainly been much more pronounced in arsenical cases than in those alcoholic cases noted before. The motor symptoms appear to me to be indistinguishable from those observed in alcoholic neuritis, and all my arsenical cases have been symmetrical, whilst I have had cases of alcoholic neuritis in which only one limb has been attacked. In some of my severe cases of arsenical neuritis there has been paralysis of rectum and bladder, a point rarely seen in alcoholic neuritis. When one considers the enormous number of people who have been drinking this beer, which has in some cases in Liverpool contained one and a half grains of arsenic to the gallon, one is bound to think that some people are more susceptible to it than others, as only a very small proportion have been attacked. It is apparent, too, that arsenic is a cumulative poison to some extent. It would seem, also, that the action of arsenic in the system is more virulent in the presence of alcohol than when given alone. With regard to the mental symptoms, I have observed drowsiness and hebetude, with great depression and desire to sleep constantly, but nothing special in the other brain symptoms compared with those due to alcohol alone. Four cases of arsenical neuritis have died, and most of the others are rapidly improving, some of the worst cases doing well; and although I have seen paralysis of the diaphragm three times in alcoholic neuritis, so far I have not noticed it in arsenical. After a careful observation of the epidemic, I have come to the conclusion that the sensory symptoms are more pronounced in arsenical neuritis than in ordinary alcoholic neuritis, and, although very severe at first, soon pass away. The motor symptoms tend more quickly to recover under treatment than the purely alcoholic cases, and most of my cases have almost completely recovered, although a few are making no progress. One patient, after desquamating in dark brown scales, had a secondary desquamation two months afterwards. In no case have I found the slightest trace of arsenic in the scales. So far as Liverpool is concerned the epidemic is at an end, and I have not had a new case of neuritis for two weeks. It is just possible that with greater care in the manufacture of beer, alcoholic neuritis may become much less frequent. *Microscopically* the nerves show marked degeneration, but nothing distinguishable from ordinary peripheral neuritis. With regard to the amount

of arsenic concerned, it was stated in court this morning in Liverpool that over three hundred pounds in weight of white arsenic was used every week in the manufacture of beer, so that one cannot be surprised at the results. With regard to treatment after the stage of depression and cardiac weakness has passed off, I have obtained excellent results from potassium iodide, grs. v, t. d. s., with extra nourishing food, and the continuous current, with massage of the affected muscles. I am making more minute investigations into the whole epidemic, and shall hope to be able to communicate something more definite at a later period.

Dr. REYNOLDS.—I thank you all very much for the kind way in which you have spoken of my discovery of the arsenical origin of these cases; I am really very much ashamed of myself that it should have gone on so long before I discovered it. On looking back it seems such a very simple thing, and I can see no reason why it was not discovered two months earlier. We were very greatly misled by our attaching too much attention to the fact of alcohol. I am willing to admit that alcoholic neuritis exists, but I am not convinced thereof. It is certain that alcoholic neuritis and alcoholic heart failure is much less common in London than in Manchester, and we always tell our students to avoid mentioning alcohol as a cause of heart failure when they go up for examination. It has now been shown that it is very difficult to get alcoholic beverages without arsenic. Sulphuric acid is largely used in the manufacture of nearly all the yeast which is obtained from brewers; it is largely present in malt, into which it enters in the drying kilns. Wines are largely contaminated with arsenic, so much so that in France they are methodically examined to ascertain its absence. I would suggest that, whereas in this present epidemic we have been seeing more the general symptoms of arsenical poisoning, it is quite possible that for many years we have only been seeing the special symptoms of very minute traces of arsenic on the nervous system. It is quite possible that very minute traces of arsenic may have a specific action on the nervous system, on the skin, etc.

I very soon found that you had to insist upon a definite answer to questions put to patients. Having found that the fingers and toes began to be affected about a fortnight after drinking the arsenicated beer—and I have one attacked a fortnight after, and then there was a history of diarrhœa and vomiting,—I did not have this history when accompanied by Dr. Luff, but one was later. The question of selenium is very interesting, and it is one that should be worked out, but as yet no observations have been possible in man, so we cannot go further in the matter. As to the tenderness of the calves, I

should have stated in my paper that the excruciating tenderness of the calves was especially associated with beri-beri or arsenic. It is not a mere ordinary tenderness, it is so great that only yesterday, when I was going down my wards with a visitor, one of these women, as soon as we got near her bed, cried out that we should not come near her, so apprehensive was she of the pain caused by examination. I know that you get pain in diphtheritic paralysis, but nothing like this. In taking the history of these drinkers, I find we are too readily satisfied with a history of spirit drinking, and we are positively pleased if we can get such an admission. Now for many years I have not rested satisfied with this confession, and when I come across a case of peripheral neuritis I have made particular inquiry as to beer. In every case I have found that beer has been drunk in large quantities. People take it because they are thirsty, and they do not count it as drink. We must not, therefore, be too ready to accept as final a history of spirit drinking in these cases, but must insist on knowing whether beer has also been taken.

THE PRESIDENT.—We who have listened to the address that has just been delivered are, I am sure, ready to admit, and it may be said the profession generally recognise, that great credit is due to the author for his early detection of the cause of the outbreak of illness that has recently occurred in certain northern districts of our country. He has placed before us this evening a most lucid and interesting account detailing the symptoms observed. I propose a hearty vote of thanks to him for his paper.